

# **PCT**

### **INTERNATIONAL SEARCH REPORT**

(PCT Article 18 and Rules 43 and 44)

``	olicant's or agent's file reference	FOR FURTHER see Notificat (Form PCT/	tion of Transmittal of International Search Report (ISA/220) as well as, where applicable, item 5 below.
	ernational application No.	International filing date (day/month/year	r) (Earliest) Priority Date (day/month/year)
PC'	T/IB 03/06281	17/11/2003	15/11/2002
Арр	olicant	<del></del>	
CH:	IRON SRL	1	
Th ac	is International Search Report has been seeding to Article 18. A copy is being t	en prepared by this International Searching ransmitted to the International Bureau.	Authority and is transmitted to the applicant
:q. —c	solding to the role for the self to see. 9 a	and morning balous, was a	To effect the months that the second of the
Th	nis International Search Report consists	s of a total of 8 sheets.	
	X It is also accompanied by	y a copy of each prior art document cited in	this report.
	Posis of the report		
1.		international coarsh was carried out on th	e basis of the international application in the
	language in which it was filed, ur	nternational search was carried out on the ntess otherwise indicated under this item.	a casis of the international application in the
	the international search	was carried out on the basis of a translation	n of the international application furnished to this
	Authority (Rule 23.1(b)).	•	
	b. With regard to any nucleotide ar was carried out on the basis of the	nd/or amino acid sequence disclosed in the sequence listing:	the international application, the international search
		onal application in written form.	
	filed together with the int	ernational application in computer readable	e form.
	furnished subsequently t	o this Authority in written form.	
	X furnished subsequently to	o this Authority in computer readble form.	
	the statement that the su international application a	bsequently furnished written sequence listi as filed has been furnished.	ing does not go beyond the disclosure in the
	X the statement that the inf furnished	ormation recorded in computer readable fo	orm is identical to the written sequence listing has been
2.	Certain claims were for	und unsearchable (See Box I).	
3.	X Unity of invention is lac	king (see Box II).	
4.	With regard to the title,	•	
		ubmitted by the applicant.	
	X the text has been establis	shed by this Authority to read as follows:	·
	UNEXPECTED SURFACE PRO	OTEINS IN NEISSERIA MENING	GITIDIS
5.		OTEINS IN NEISSERIA MENIN	GITIDIS
5.	With regard to the abstract,		GITIDIS
<b>5.</b>	With regard to the abstract,  X the text is approved as su the text has been established.	ubmitted by the applicant.	thority as it appears in Boy III. The applicant may
5.	With regard to the abstract,  X the text is approved as su the text has been established.	ubmitted by the applicant. shed, according to Rule 38.2(b), by this Aut e date of mailing of this international search	
	With regard to the abstract,  The text is approved as sure the text has been establis within one month from the	ubmitted by the applicant. shed, according to Rule 38.2(b), by this Aut e date of mailing of this international search lished with the abstract is Figure No.	thority as it appears in Box III. The applicant may, h report, submit comments to this Authority.
	With regard to the abstract,  X the text is approved as sure the text has been establis within one month from the text that the text has been established. The figure of the drawings to be published.	ubmitted by the applicant. shed, according to Rule 38.2(b), by this Aut e date of mailing of this international search lished with the abstract is Figure No. icant.	thority as it appears in Boy III. The applicant may



Box I	Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)
This Inte	ernational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1.	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
2.	Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This Inte	ernational Searching Authority found multiple inventions in this international application, as follows:
	see additional sheet
1.	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. X	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  1-5 (all partly)
Remark	The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.

### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Inventions 1-158: claims 1-5 (all partly)

#### Inventions 1-158:

A compostion comprising (a) outer-membrane vesicles (OMV's) prepared from a first strain of Neisseria meningitidis and (b) one or more proteins which are present in OMV's prepared froma second strain of Neisseria meningitidis, but which are not present in OMV's prepared from said first strain. Furthermore the specification of (b), the use of OMV's of genetically-modified strains of Neisseria meningitidis comprising proteins not present in OMV's prior to modification and furthermore the specification of the protein of (b) as set out in claims 4 or 5. Each of the inventions 1-158 specifically and respectively relates to one of the proteins set out in claims 4 or 5 e.g. for invention 1, NMB0007 etc... to invention 158, NMB2159.

Inventions 159-375: claims 6-8 (all partly)

#### Inventions 159-375:

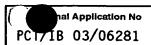
A lipid bilayer including each and respectively a protein comprising an amino acid sequence selected from the group consisting of SEQ ID NO's: 1-217 or diverse variants, fragments or hybrids thereof. Furthermore the specification of the lipid bilayer and the said lipid bilayer which does not include some native membrane components. Each of the inventions 159-217 specifically and respectively relates to one of the proteins set out in SEQ ID NO's 1-217 e.g. for invention 159, SEQ ID NO: 1 etc... to invention 375, SEQ ID NO: 217.

Inventions 376-592: claims 10-13 (all partly)

### Inventions 376-592:

A protein comprising each and respectively an amino acid sequence selected from the group consisting of SEQ ID NO's: 1-217 or diverse variants, fragments or hybrids thereof. Furthermore a nucleic acid encoding each of said proteins. Each of the inventions 376-592 specifically and respectively relates to one of the proteins set out in SEQ ID NO's 376-593 e.g. for invention 376, SEQ ID NO: 1 etc... to invention 593, SEQ ID NO: 217.

## INTECNATIONAL SEARCH REPORT



A. CLAS	SSIFICATION	<b>OF SUBJECT</b>	MATTER	
IPC 7	7 A61K	(39/095	C07K14	/22

According to International Patent Classification (IPC) or to both national classification and IPC

#### B. FIELDS SEARCHED

• • •

 $\begin{array}{ll} \mbox{Minimum documentation searched (classification system followed by classification symbols)} \\ \mbox{IPC 7} & \mbox{A61K} \end{array}$ 

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, MEDLINE, WPI Data, PAJ, Sequence Search

C. DOCUM	ENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with Indication, where appropriate, of the	e relevant passages	Relevant to claim No.
X	CLAASSEN I ET AL: "Production characterization and control or Neisseria meningitidis hexaval outer membrane protein contain vaccine" VACCINE, BUTTERWORTH SCIENTIFIC GUILDFORD, GB, vol. 14, no. 10, 1 July 1996 (pages 1001–1008, XP004057632 ISSN: 0264-410X	f a ent class 1 ing vesicle C.	1-3
	page 1002, left-hand column same citations		
		<b>-/</b>	
X Furt	her documents are listed in the continuation of box C.	Patent family members are liste	d in annex.
<u> </u>			
*A* docum consid *E* earlier filing	ent defining the general state of the art which is not dered to be of particular relevance document but published on or after the international date ent which may throw doubts on priority claim(s) or is cited to establish the publication date of another n or other special reason (as specified) ent referring to an oral disclosure, use, exhibition or	<ul> <li>"T" later document published after the in or priority date and not in conflict we cited to understand the principle or invention</li> <li>"X" document of particular relevance; the cannot be considered novel or can involve an inventive step when the</li> <li>"Y" document of particular relevance; the cannot be considered to involve an document is combined with one or mostly supplementation being obtained.</li> </ul>	ith the application but theory underlying the eclaimed invention not be considered to document is taken alone eclaimed invention inventive step when the
which citation "O" document other "P" document of the cument of the cume	means ent published prior to the international filing date but han the priority date clained	in the art.  *&* document member of the same pate	nt family
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which citation of the of the of the of the	means ent published prior to the international filing date but han the priority date claimed	in the art.  *&* document member of the same pate	

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### INTERNATIONAL SEARCH REPORT





		PC171B 03/06281		
C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT  Category Citation of document, with indication, where appropriate, of the relevant passages  Relevant to claim No.				
Calegory	Chains of Counteris, with indication, where appropriate, of the relevant passages	ricievant to Claim 140.		
A :	-& VAN DER LEY P ET AL: "Construction of Neisseria meningitidis strains carrying multiple chromosomal copies of the porA gene for use in the production of a multivalent outer membrane vesicle vaccine" VACCINE, BUTTERWORTH SCIENTIFIC. GUILDFORD, GB, vol. 13, no. 4, 1995, pages 401-407, XP004057740 ISSN: 0264-410X page 404, right-hand column, paragraph 2 page 405, right-hand column, paragraph 1			
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X	WO 00/25811 A (GORRINGE ANDREW RICHARD; HUDSON MICHAEL JOHN (GB); MICROBIOLOGICAL) 11 May 2000 (2000-05-11) page 2 - page 6	1,2		
Y	NORAIS NATHALIE ET AL: "Combined automated PCR cloning, in vitro transcription/translation and two-dimensional electrophoresis for bacterial proteome analysis" PROTEOMICS, vol. 1, no. 11, November 2001 (2001-11), pages 1378-1389, XP009032238 ISSN: 1615-9853 page 1382, left-hand column, paragraph 1 - page 1383, left-hand column, paragraph 1; table 2	4		
Y	DATABASE UNIPROT 'Online! EBI; 1 October 2000 (2000-10-01), TETTELIN ET AL.: "Cell division ATP binding protein FtsE" XP002284894 Database accession no. Q9K1R3 the whole document	4		
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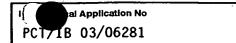
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		PCT/1B 03/06281
C.(Continua	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GRIFANTINI R ET AL: "Previously unrecognized vaccine candidates against group B meningococcus identified by DNA microarrays" NATURE BIOTECHNOLOGY, NATURE PUBLISHING, US,	·
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A	PIZZA M ET AL: "IDENTIFICATION OF VACCINE CANDIDATES AGAINST SEROGROUP B MENINGOCOCCUS BY WHOLE-GENOME SEQUENCING" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE, US, vol. 287, no. 5459, 10 March 2000 (2000-03-10), pages 1816-1820, XP000986271 ISSN: 0036-8075 page 1817 - page 1818; table 1	
A	TETTELIN H ET AL: "COMPLETE GENOME SEQUENCE OF NEISSERIA MENINGITIDIS SEROGROUP B STRAIN MC58" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE, US, vol. 287, 2000, pages 1809-1815, XP000914963 ISSN: 0036-8075 the whole document	
A	JOLLEY KEITH A ET AL: "Immunization with recombinant Opc outer membrane protein from Neisseria meningitidis: Influence of sequence variation and levels of expression on the bactericidal immune response against meningococci" INFECTION AND IMMUNITY, vol. 69, no. 6, June 2001 (2001-06), pages 3809-3916, XP002284891 ISSN: 0019-9567 page 3810	
Α	WRIGHT J CLAIRE ET AL: "Immunization with the recombinant PorB outer membrane protein induces a bactericidal immune response against Neisseria meningitidis" INFECTION AND IMMUNITY, vol. 70, no. 8, August 2002 (2002-08), pages 4028-4034, XP002284892 ISSN: 0019-9567 page 4029	

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	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
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4	WO 01/09350 A (DALEMANS WILFRIED L J;SMITHKLINE BEECHAM BIOLOG (BE); THIRY GEORG) 8 February 2001 (2001-02-08) examples 3-5	

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hal Application No PCT/IB 03/06281

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